

We claim:

1. A stable fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
- (b) associated with the surface thereof at least one surface stabilizer, wherein the surface stabilizer is not PEG-derivatized vitamin E.

2. The composition of claim 1, wherein the fibrate is fenofibrate or a salt thereof.

3. The composition of claim 1, wherein the fibrate is selected from the group consisting of a crystalline phase, an amorphous phase, a semi-crystalline phase, a semi-amorphous phase, and mixtures thereof.

4. The composition of claim 1, wherein the effective average particle size of the fibrate particles is selected from the group consisting of less than about 1900 nm, less than about 1800 nm, less than about 1700 nm, less than about 1600 nm, less than about 1500 nm, less than about 1400 nm, less than about 1300 nm, less than about 1200 nm, less than about 1100 nm, less than about 1000 nm, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 200 nm, less than about 100 nm, less than about 75 nm, and less than about 50 nm.

5. The composition of claim 4, wherein the fibrate is fenofibrate or a salt thereof.

6. The composition of claim 1, wherein the composition is formulated for administration selected from the group consisting of oral, pulmonary, rectal, ophthalmic, colonic, parenteral, intracisternal, intravaginal, intraperitoneal, local, buccal, nasal, and topical administration.

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7. The composition of claim 1 formulated into a dosage form selected from the group consisting of liquid dispersions, oral suspensions, gels, aerosols, ointments, creams, controlled release formulations, fast melt formulations, lyophilized formulations, tablets, capsules, delayed release formulations, extended release formulations, pulsatile release formulations, and mixed immediate release and controlled release formulations.

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8. The composition of claim 1, wherein the composition further comprises one or more pharmaceutically acceptable excipients, carriers, or a combination thereof.

9. The composition of claim 1, wherein the fibrate or a salt thereof is present in an amount selected from the group consisting of from about 99.5% to about 0.001%, from about 95% to about 0.1%, and from about 90% to about 0.5%, by weight, based on the total combined weight of the fibrate or a salt thereof and at least one surface stabilizer, not including other excipients.

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10. The composition of claim 1, wherein the at least one surface stabilizer is present in an amount selected from the group consisting of from about 0.5% to about 99.999% by weight, from about 5.0% to about 99.9% by weight, and from about 10% to about 99.5% by weight, based on the total combined dry weight of the fibrate or a salt thereof and at least one surface stabilizer, not including other excipients.

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11. The composition of claim 1, comprising at least one primary surface stabilizer and at least one secondary surface stabilizer.

12. The composition of claim 1, wherein the surface stabilizer is selected from the group consisting of an anionic surface stabilizer, a cationic surface stabilizer, a zwitterionic surface stabilizer, and an ionic surface stabilizer.

5 13. The composition of claim 12, wherein the fibrate is fenofibrate or a salt thereof.

14. The composition of claim 12, wherein the at least one surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein,  
10 phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates,  
15 colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hypromellose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hypromellose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde,  
20 poloxamers; poloxamines, a charged phospholipid, dioctylsulfosuccinate, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfate, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), decanoyl-N-methylglucamide; n-decyl  $\beta$ -D-glucopyranoside; n-decyl  $\beta$ -D-maltopyranoside; n-dodecyl  $\beta$ -D-glucopyranoside; n-dodecyl  $\beta$ -D-maltoside; heptanoyl-N-methylglucamide; n-heptyl-  
25  $\beta$ -D-glucopyranoside; n-heptyl  $\beta$ -D-thioglucoside; n-hexyl  $\beta$ -D-glucopyranoside; nonanoyl-N-methylglucamide; n-nonyl  $\beta$ -D-glucopyranoside; octanoyl-N-methylglucamide; n-octyl- $\beta$ -D-glucopyranoside; octyl  $\beta$ -D-thioglucopyranoside; lysozyme, PEG-phospholipid, PEG-cholesterol, PEG-cholesterol derivative, PEG-vitamin A, and random copolymers of vinyl acetate and vinyl pyrrolidone.

15. The composition of claim 12, wherein the at least one cationic surface stabilizer is selected from the group consisting of a polymer, a biopolymer, a polysaccharide, a cellulosic, an alginate, a nonpolymeric compound, and a phospholipid.

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16. The composition of claim 12, wherein the surface stabilizer is selected from the group consisting of cationic lipids, polymethylmethacrylate trimethylammonium bromide, sulfonium compounds, polyvinylpyrrolidone-2-dimethylaminoethyl methacrylate dimethyl sulfate, hexadecyltrimethyl ammonium bromide, phosphonium compounds, quarternary ammonium compounds, benzyl-di(2-chloroethyl)ethylammonium bromide, coconut trimethyl ammonium chloride, coconut trimethyl ammonium bromide, coconut methyl dihydroxyethyl ammonium chloride, coconut methyl dihydroxyethyl ammonium bromide, decyl triethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride bromide, C<sub>12-15</sub>dimethyl hydroxyethyl ammonium chloride, C<sub>12-15</sub>dimethyl hydroxyethyl ammonium chloride bromide, coconut dimethyl hydroxyethyl ammonium chloride, coconut dimethyl hydroxyethyl ammonium bromide, myristyl trimethyl ammonium methyl sulphate, lauryl dimethyl benzyl ammonium chloride, lauryl dimethyl benzyl ammonium bromide, lauryl dimethyl (ethenoxy)<sub>4</sub> ammonium chloride, lauryl dimethyl (ethenoxy)<sub>4</sub> ammonium bromide, N-alkyl (C<sub>12-18</sub>)dimethylbenzyl ammonium chloride, N-alkyl (C<sub>14-18</sub>)dimethyl-benzyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium chloride monohydrate, dimethyl didecyl ammonium chloride, N-alkyl and (C<sub>12-14</sub>) dimethyl 1-naphthylmethyl ammonium chloride, trimethylammonium halide, alkyl-trimethylammonium salts, dialkyl-dimethylammonium salts, lauryl trimethyl ammonium chloride, ethoxylated alkyamidoalkyldialkylammonium salt, an ethoxylated trialkyl ammonium salt, dialkylbenzene dialkylammonium chloride, N-didecyldimethyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium, chloride monohydrate, N-alkyl(C<sub>12-14</sub>) dimethyl 1-naphthylmethyl ammonium chloride, dodecyldimethylbenzyl ammonium chloride, dialkyl benzenealkyl ammonium chloride, lauryl trimethyl ammonium chloride, alkylbenzyl methyl ammonium chloride, alkyl

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benzyl dimethyl ammonium bromide, C<sub>12</sub> trimethyl ammonium bromides, C<sub>15</sub> trimethyl ammonium bromides, C<sub>17</sub> trimethyl ammonium bromides, dodecylbenzyl triethyl ammonium chloride, poly-diallyldimethylammonium chloride (DADMAC), dimethyl ammonium chlorides, alkyldimethylammonium halogenides, tricetyl methyl ammonium chloride, decyltrimethylammonium bromide, dodecyltriethylammonium bromide, tetradecyltrimethylammonium bromide, methyl trioctylammonium chloride, POLYQUAT 10™, tetrabutylammonium bromide, benzyl trimethylammonium bromide, choline esters, benzalkonium chloride, stearalkonium chloride compounds, cetyl pyridinium bromide, cetyl pyridinium chloride, halide salts of quaternized polyoxyethylalkylamines, MIRAPOL™, ALKAQUAT™, alkyl pyridinium salts; amines, amine salts, amine oxides, imide azolinium salts, protonated quaternary acrylamides, methylated quaternary polymers, and cationic guar.

17. The composition of any of claims 12, 15, or 16, wherein the composition is bioadhesive.

18. The composition of claim 17, wherein the fibrate is fenofibrate or a salt thereof.

19. The composition of claim 1, comprising hypromellose, dioctyl sodium sulfosuccinate, and sodium lauryl sulfate as surface stabilizers.

20. The composition of claim 19, wherein the fibrate is fenofibrate or a salt thereof.

21. The composition of claim 1, wherein the composition exhibits a T<sub>max</sub> selected from the group consisting of less than about 6 hours, less than about 5 hours, less than about 4 hours, less than about 3 hours, less than about 2 hours, less than about 1 hour, and less than about 30 minutes after administration to fasting subjects.

22. The composition of claim 1, wherein in comparative pharmacokinetic testing with a TRICOR<sup>®</sup> 160 mg tablet or 200 mg capsule, which are standard commercial formulations of microcrystalline fenofibrate, the composition of claim 1 exhibits a T<sub>max</sub> selected from the group consisting of less than about 90%, less than about 80%, less than about 70%, less than about 50%, less than about 30%, and less than about 25% of the T<sub>max</sub> exhibited by the TRICOR<sup>®</sup> tablet or capsule.

23. The composition of claim 1 which does not produce significantly different absorption levels when administered under fed as compared to fasting conditions.

24. The composition of claim 23, wherein the difference in absorption of the fibrate composition of the invention, when administered in the fed versus the fasted state, is selected from the group consisting of less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, and less than about 3%.

25. The composition of claim 23 or 24, wherein the fibrate is fenofibrate or a salt thereof.

26. The fibrate composition of claim 1, additionally comprising one or more active agents selected from the group consisting of HMG CoA reductase inhibitors and antihypertensives.

27. A composition comprising a fibrate or a salt thereof, wherein the pharmacokinetic profile of the fibrate or a salt thereof is not significantly affected by the fed or fasted state of a subject ingesting the composition, when administered to a human.

28. The composition of claim 27, wherein the fibrate is fenofibrate or a salt thereof.

29. A composition comprising a fibrate or a salt thereof, wherein administration of the composition to a subject in a fasted state is bioequivalent to administration of the composition to a subject in a fed state, when administered to a human.

30. The composition of claim 29, wherein the fibrate is fenofibrate or a salt thereof.

31. A composition comprising about 145 mg of fenofibrate or a salt thereof and exhibiting minimal or no food effect when administered to a human.

32. A composition comprising about 48 mg of fenofibrate or a salt thereof and exhibiting minimal or no food effect when administered to a human.

33. A composition comprising fenofibrate or a salt thereof and having a  $C_{\max}$  under fasted conditions which is greater than the  $C_{\max}$  under high fat fed conditions when administered to a human.

34. A composition comprising a fibrate or a salt thereof, wherein administration of the composition to a subject in a fasted state is bioequivalent to administration of the composition to a subject in a fed state, wherein "bioequivalency" is established by a 90% Confidence Interval of between 0.80 and 1.25 for both  $C_{\max}$  and AUC, when administered to a human.

35. A composition comprising a fibrate or a salt thereof, wherein administration of the composition to a subject in a fasted state is bioequivalent to administration of the composition to a subject in a fed state, wherein "bioequivalency" is established by a 90% Confidence Interval of between 0.80 and 1.25 for AUC and a 90% Confidence Interval of between 0.70 to 1.43 for  $C_{\max}$ , when administered to a human.

36. A composition comprising a fibrate or a salt thereof, wherein the composition has a  $T_{\max}$  selected from the group consisting of less than about 6 hours, less than about 5 hours, less than about 4 hours, less than about 3 hours, less than about 2 hours, less than about 1 hour, and less than about 30 minutes after administration to fasting subjects.

37. The composition of claim 36, wherein the fibrate is fenofibrate or a salt thereof.

38. A composition comprising fenofibrate or a salt thereof, wherein in comparative pharmacokinetic testing with a TRICOR<sup>®</sup> 160 mg tablet or 200 mg capsule, which are standard commercial formulations of microcrystalline fenofibrate, the fenofibrate composition exhibits a  $T_{\max}$  selected from the group consisting of less than about 90%, less than about 80%, less than about 70%, less than about 50%, less than about 30%, and less than about 25% of the  $T_{\max}$  exhibited by the standard commercial microcrystalline fenofibrate formulations.

39. A fenofibrate composition comprising fenofibrate or a salt thereof, which when administered to a human as a dose of about 160 mg presents an AUC of about 139  $\mu\text{g/mL.h}$ .

40. A stable fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have a particle size in which the  $D_{99}$  is less than about 500 nm; and
- (b) associated with the surface thereof at least one surface stabilizer.



41. A stable fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have a particle size in which the  $D_{50}$  is less than about 350 nm; and
- (b) associated with the surface thereof at least one surface stabilizer.

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42. A stable fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have a mean particle size of less than about 100 nm; and
- (b) associated with the surface thereof at least one surface stabilizer.

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43. A fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
- (b) associated with the surface thereof at least one surface stabilizer, wherein said surface stabilizer is not a phospholipid.

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44. A stable fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
- (b) associated with the surface thereof at least one surface stabilizer, wherein said surface stabilizer is categorized by the U.S. Food and Drug Administration as GRAS.

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45. A fibrate composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
- (b) associated with the surface thereof at least one surface stabilizer selected from the group consisting of hypromellose, docusate sodium, Plasdone® S630, HPC-SL, sodium lauryl sulfate, and combinations thereof,

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wherein the composition does not comprise PEG-derivatized vitamin E.

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46. A fibrate composition comprising:
- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
  - 5 (b) associated with the surface thereof dioctyl sodium sulfosuccinate and hypromellose;
- wherein the composition does not comprise PEG-derivatized vitamin E.

47. The composition of claim 46, wherein the fibrate is fenofibrate or a salt  
10 thereof.

48. The composition of claim 46, further comprising sodium lauryl sulfate.

49. The composition of claim 46, wherein the pharmacokinetic profile of the  
15 fibrate or a salt thereof is not affected by the fed or fasted state of a subject ingesting the composition.

50. The composition of claim 46, wherein administration of the composition to  
a subject in a fasted state is bioequivalent to administration of the composition to a  
20 subject in a fed state.

51. A fibrate composition comprising:
- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
  - 25 (b) associated with the surface thereof at least one surface stabilizer;
- wherein the composition is bioadhesive.

52. A stable fibrate composition comprising a fibrate or a salt thereof, wherein  
within about 5 minutes at least about 20% of the composition is dissolved, wherein

dissolution is measured in a media which is discriminating and wherein the rotating blade method (European Pharmacopoeia) is used to measure dissolution.

53. The composition of claim 52, in which at least about 30% of the  
5 composition is dissolved within about 5 minutes.

54. The composition of claim 53, in which at least about 40% of the  
composition is dissolved within about 5 minutes.

10 55. The composition of claim 52, wherein the fibrate is fenofibrate or a salt  
thereof.

56. The composition of claim 52, wherein upon redispersion the fibrate  
particles have an effective average particle size of less than about 2 microns.

15 57. A stable fibrate composition comprising a fibrate or a salt thereof, wherein  
within about 10 minutes at least about 40% of the composition is dissolved, wherein  
dissolution is measured in a media which is discriminating and wherein the rotating blade  
method (European Pharmacopoeia) is used to measure dissolution.

20 58. The composition of claim 57, wherein at least about 50%, about 60%,  
about 70%, or about 80% of the composition is dissolved within about 10 minutes.

25 59. The composition of claim 57, wherein the fibrate is fenofibrate or a salt  
thereof.

60. The composition of claim 57, wherein upon redispersion the fibrate  
particles have an effective average particle size of less than about 2 microns.

61. A stable fibrate composition comprising a fibrate or a salt thereof, wherein within about 20 minutes at least about 70% of the composition is dissolved, wherein dissolution is measured in a media which is discriminating and wherein the rotating blade method (European Pharmacopoeia) is used to measure dissolution.

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62. The composition of claim 61, wherein at least about 80%, about 90%, or about 100% of the composition is dissolved within about 20 minutes.

63. The composition of claim 61, wherein the fibrate is fenofibrate or a salt thereof.

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64. The composition of claim 61, wherein upon redispersion the fibrate particles have an effective average particle size of less than about 2 microns.

15 65. A fibrate composition comprising:

(a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and

(b) associated with the surface thereof at least one surface stabilizer,

wherein upon administration the composition redisperses such that the fibrate particles have an effective average particle size selected from the group consisting of less than about 2000 nm, less than about 1900 nm, less than about 1800 nm, less than about 1700 nm, less than about 1600 nm, less than about 1500 nm, less than about 1400 nm, less than about 1300 nm, less than about 1200 nm, less than about 1100 nm, less than about 1000 nm, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 200 nm, less than about 150 nm, less than about 100 nm, less than about 75 nm, and less than about 50 nm.

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66. A fibrate composition comprising

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
- (b) associated with the surface thereof at least one surface stabilizer,

5 wherein the composition redisperses in a biorelevant media such that the fibrate particles have an effective average particle size selected from the group consisting of less than about 2 microns, less than about 1900 nm, less than about 1800 nm, less than about 1700 nm, less than about 1600 nm, less than about 1500 nm, less than about 1400 nm, less than about 1300 nm, less than about 1200 nm, less than about 1100 nm, less than  
10 about 1000 nm, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 200 nm, less than about 150 nm, less than about 100 nm, less than about 75 nm, and less than about 50 nm.

15 67. A fenofibrate composition comprising a dosage of about 145 mg of particles of fenofibrate or a salt thereof, wherein:

- (a) said dosage is therapeutically effective; and
- (b) the composition is bioequivalent to a TRICOR<sup>®</sup> 160 mg tablet or 200 mg capsule, wherein bioequivalency is established by a 90% Confidence  
20 Interval of between 0.80 and 1.25 for both  $C_{max}$  and AUC or a 90% Confidence Interval of between 0.80 and 1.25 for AUC and a 90% Confidence Interval of between 0.70 to 1.43 for  $C_{max}$ , when administered to a human.

25 68. The composition of claim 67, wherein the fenofibrate particles have associated with the surface thereof at least one surface stabilizer.

69. The composition of claim 67, wherein the fenofibrate particles have an effective average particle size of less than about 2000 nm.

70. The composition of claim 67, wherein the dosage form is about 10% smaller than the TRICOR<sup>®</sup> 160 mg tablet or 200 mg capsule.

71. A fenofibrate composition comprising a dosage of 48 mg of particles of fenofibrate or a salt thereof, wherein:

- (a) said dosage is therapeutically effective; and
- (b) the composition is bioequivalent to a TRICOR<sup>®</sup> 54 mg tablet, wherein bioequivalency is established by a 90% Confidence Interval of between 0.80 and 1.25 for both  $C_{\max}$  and AUC or a 90% Confidence Interval of between 0.80 and 1.25 for AUC and a 90% Confidence Interval of between 0.70 to 1.43 for  $C_{\max}$ , when administered to a human.

72. The composition of claim 71, wherein the fenofibrate particles have associated with the surface thereof at least one surface stabilizer.

73. The composition of claim 71, wherein the fenofibrate particles have an effective average particle size of less than about 2000 nm.

74. The composition of claim 71, wherein the dosage form is about 10% smaller than the TRICOR<sup>®</sup> 160 mg tablet or 200 mg capsule.

75. A fenofibrate composition comprising the following:

- (a) about 50 to about 500 g/kg fenofibrate or a salt thereof;
- (b) about 10 to about 70 g/kg hypromellose;
- (c) about 1 to about 10 g/kg docusate sodium;
- (d) about 100 to about 500 g/kg sucrose;
- (e) about 1 to about 40 g/kg sodium lauryl sulfate;
- (f) about 50 to about 400 g/kg lactose monohydrate;
- (g) about 50 to about 300 g/kg silicified microcrystalline cellulose;
- (h) about 20 to about 300 g/kg crospovidone; and
- (i) about 0.5 to about 5 g/kg magnesium stearate.

76. The composition of claim 75, further comprising a coating agent.

77. A fenofibrate composition comprising the following:

- (a) about 100 to about 300 g/kg fenofibrate or a salt thereof;
- (b) about 30 to about 50 g/kg hypromellose;
- (c) about 0.5 to about 10 g/kg docusate sodium;
- (d) about 100 to about 300 g/kg sucrose;
- (e) about 1 to about 30 g/kg sodium lauryl sulfate;
- (f) about 100 to about 300 g/kg lactose monohydrate;
- (g) about 50 to about 200 g/kg silicified microcrystalline cellulose;
- (h) about 50 to about 200 g/kg crospovidone; and
- (i) about 0.5 to about 5 g/kg magnesium stearate.

78. The composition of claim 77, further comprising a coating agent.

79. A fenofibrate composition comprising the following:

- (a) about 200 to about 225 g/kg fenofibrate or a salt thereof;
- (b) about 42 to about 46 g/kg hypromellose;
- (c) about 2 to about 6 g/kg docusate sodium;
- (d) about 200 to about 225 g/kg sucrose;
- (e) about 12 to about 18 g/kg sodium lauryl sulfate;
- (f) about 200 to about 205 g/kg lactose monohydrate;
- (g) about 130 to about 135 g/kg silicified microcrystalline cellulose;
- (h) about 112 to about 118 g/kg crospovidone; and
- (i) about 0.5 to about 3 g/kg magnesium stearate.

80. The composition of claim 79, further comprising a coating agent.

81. A fenofibrate composition comprising the following:

- (a) about 119 to about 224 g/kg fenofibrate or a salt thereof;
- (b) about 42 to about 46 g/kg hypromellose;
- (c) about 2 to about 6 g/kg docusate sodium;
- (d) about 119 to about 224 g/kg sucrose;
- (e) about 12 to about 18 g/kg sodium lauryl sulfate;
- (f) about 119 to about 224 g/kg lactose monohydrate;
- (g) about 129 to about 134 g/kg silicified microcrystalline cellulose;
- (h) about 112 to about 118 g/kg crospovidone; and
- (i) about 0.5 to about 3 g/kg magnesium stearate.

82. The composition of claim 81, further comprising a coating agent.



83. A method of making a fibrate composition comprising contacting particles of a fibrate or a salt thereof with at least one surface stabilizer for a time and under conditions sufficient to provide a fibrate composition having an effective average particle size of less than about 2000 nm, wherein the surface stabilizer is not PEG-derivatized vitamin E,

84. The method of claim 83, wherein the fibrate is fenofibrate or a salt thereof.

85. The method of claim 83, wherein said contacting comprises grinding.

86. The method of claim 85, wherein said grinding comprises wet grinding.

87. The method of claim 83, wherein said contacting comprises homogenizing.

88. The method of claim 83, wherein said contacting comprises:

- (a) dissolving the particles of a fibrate or a salt thereof in a solvent;
- (b) adding the resulting fibrate solution to a solution comprising at least one surface stabilizer; and
- (c) precipitating the solubilized fibrate having at least one surface stabilizer adsorbed on the surface thereof by the addition thereto of a non-solvent.

89. The method of claim 83, wherein the fibrate or a salt thereof is selected from the group consisting of a crystalline phase, an amorphous phase, a semi-crystalline phase, a semi-amorphous phase, and mixtures thereof.

90. The method of claim 83, wherein the effective average particle size of the fibrate particles is selected from the group consisting of less than about 1900 nm, less than about 1800 nm, less than about 1700 nm, less than about 1600 nm, less than about 1500 nm, less than about 1000 nm, less than about 1400 nm, less than about 1300 nm,

less than about 1200 nm, less than about 1100 nm, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 200 nm, less than about 100 nm, less than about 75 nm, and less than about 50 nm.

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91. The method of claim 83, wherein the composition is formulated for administration selected from the group consisting of oral, pulmonary, rectal, ophthalmic, colonic, parenteral, intracisternal, intravaginal, intraperitoneal, local, buccal, nasal, and topical administration.

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92. The method of claim 83, wherein the composition further comprises one or more pharmaceutically acceptable excipients, carriers, or a combination thereof.

93. The method of claim 83, wherein the fibrate or a salt thereof is present in an amount selected from the group consisting of from about 99.5% to about 0.001%, from about 95% to about 0.1%, and from about 90% to about 0.5%, by weight, based on the total combined weight of the fibrate or a salt thereof and at least one surface stabilizer, not including other excipients.

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94. The method of claim 83, wherein the at least one surface stabilizer is present in an amount selected from the group consisting of from about 0.5% to about 99.999%, from about 5.0% to about 99.9%, and from about 10% to about 99.5% by weight, based on the total combined dry weight of the fibrate or a salt thereof and at least one surface stabilizer, not including other excipients.

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95. The method of claim 83, comprising at least one primary surface stabilizer and at least one secondary surface stabilizer.

96. The method of claim 83, wherein the surface stabilizer is selected from the group consisting of an anionic surface stabilizer, a cationic surface stabilizer, a zwitterionic surface stabilizer, and an ionic surface stabilizer.

5           97. The method of claim 96, wherein the at least one surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers,  
10 polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hypromellose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hypromellose phthalate, noncrystalline cellulose,  
15 magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde, poloxamers; poloxamines, a charged phospholipid, dioctylsulfosuccinate, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfate, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), decanoyl-N-methylglucamide; n-decyl  $\beta$ -D-glucopyranoside; n-decyl  $\beta$ -D-maltopyranoside; n-dodecyl  $\beta$ -D-glucopyranoside; n-dodecyl  $\beta$ -D-maltoside; heptanoyl-N-methylglucamide; n-heptyl- $\beta$ -D-glucopyranoside; n-heptyl  $\beta$ -D-thiogluconoside; n-hexyl  $\beta$ -D-glucopyranoside; nonanoyl-N-methylglucamide; n-nonyl  $\beta$ -D-glucopyranoside; octanoyl-N-methylglucamide; n-octyl- $\beta$ -D-glucopyranoside; octyl  $\beta$ -D-thiogluconopyranoside;  
20 lysozyme, PEG-phospholipid, PEG-cholesterol, PEG-cholesterol derivative, PEG-vitamin A, PEG-vitamin E, and random copolymers of vinyl acetate and vinyl pyrrolidone.

98. The method of claim 96, wherein the at least one cationic surface stabilizer is selected from the group consisting of a polymer, a biopolymer, a polysaccharide, a cellulosic, an alginate, a nonpolymeric compound, and a phospholipid.

5 99. The method of claim 96, wherein the surface stabilizer is selected from the group consisting of cationic lipids, polymethylmethacrylate trimethylammonium bromide, sulfonium compounds, polyvinylpyrrolidone-2-dimethylaminoethyl methacrylate dimethyl sulfate, hexadecyltrimethyl ammonium bromide, phosphonium compounds, quaternary ammonium compounds, benzyl-di(2-chloroethyl)ethylammonium bromide, 10 coconut trimethyl ammonium chloride, coconut trimethyl ammonium bromide, coconut methyl dihydroxyethyl ammonium chloride, coconut methyl dihydroxyethyl ammonium bromide, decyl triethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride bromide, C<sub>12-15</sub>dimethyl hydroxyethyl ammonium chloride, C<sub>12-15</sub>dimethyl hydroxyethyl ammonium chloride 15 bromide, coconut dimethyl hydroxyethyl ammonium chloride, coconut dimethyl hydroxyethyl ammonium bromide, myristyl trimethyl ammonium methyl sulphate, lauryl dimethyl benzyl ammonium chloride, lauryl dimethyl benzyl ammonium bromide, lauryl dimethyl (ethenoxy)<sub>4</sub> ammonium chloride, lauryl dimethyl (ethenoxy)<sub>4</sub> ammonium bromide, N-alkyl (C<sub>12-18</sub>)dimethylbenzyl ammonium chloride, N-alkyl (C<sub>14-18</sub>)dimethyl- 20 benzyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium chloride monohydrate, dimethyl didecyl ammonium chloride, N-alkyl and (C<sub>12-14</sub>) dimethyl 1-naphthylmethyl ammonium chloride, trimethylammonium halide, alkyl-trimethylammonium salts, dialkyl-dimethylammonium salts, lauryl trimethyl ammonium chloride, ethoxylated alkyamidoalkyldialkylammonium salt, an ethoxylated trialkyl 25 ammonium salt, dialkylbenzene dialkylammonium chloride, N-didecyldimethyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium, chloride monohydrate, N-alkyl(C<sub>12-14</sub>) dimethyl 1-naphthylmethyl ammonium chloride, dodecyldimethylbenzyl ammonium chloride, dialkyl benzenealkyl ammonium chloride, lauryl trimethyl ammonium chloride, alkylbenzyl methyl ammonium chloride, alkyl benzyl dimethyl 30 ammonium bromide, C<sub>12</sub> trimethyl ammonium bromides, C<sub>15</sub> trimethyl ammonium

bromides, C<sub>17</sub> trimethyl ammonium bromides, dodecylbenzyl triethyl ammonium chloride, poly-diallyldimethylammonium chloride (DADMAC), dimethyl ammonium chlorides, alkyl dimethyl ammonium halogenides, tricetyl methyl ammonium chloride, decyltrimethylammonium bromide, dodecyltriethylammonium bromide,  
5 tetradecyltrimethylammonium bromide, methyl trioctylammonium chloride, POLYQUAT 10™, tetrabutylammonium bromide, benzyl trimethylammonium bromide, choline esters, benzalkonium chloride, stearylalkonium chloride compounds, cetyl pyridinium bromide, cetyl pyridinium chloride, halide salts of quaternized polyoxyethylalkylamines, MIRAPOL™, ALKAQUAT™, alkyl pyridinium salts; amines, amine salts, amine oxides,  
10 imide azolinium salts, protonated quaternary acrylamides, methylated quaternary polymers, and cationic guar.

100. The method of any of claims 96, 98, or 99, wherein the composition is bioadhesive.

15 101. The method of claim 83, wherein the composition comprises hypromellose, dioctyl sodium sulfosuccinate, and sodium lauryl sulfate as surface stabilizers.

20 102. A method of making a fibrate composition comprising contacting particles of a fibrate or a salt thereof with at least one surface stabilizer for a time and under conditions sufficient to provide a fibrate composition having an effective average particle size of less than about 2000 nm, wherein if heat is utilized during the method the temperature is kept below the melting point, or depressed melting point, of the fibrate.

103. A method of treating a subject in need comprising administering to the subject an effective amount of a composition comprising:

- (a) particles of a fibrate or a salt thereof, wherein the fibrate particles have an effective average particle size of less than about 2000 nm; and
- (b) at least one surface stabilizer associated with the surface of the fibrate particles, wherein the surface stabilizer is not PEG-derivatized vitamin E.

104. The method of claim 103, wherein the fibrate is fenofibrate or a salt thereof.

105. The method of claim 103, wherein a maximum blood plasma concentration of the fibrate is attained in a time selected from the group consisting of less than about 6 hours, less than about 5 hours, less than about 4 hours, less than about 3 hours, less than about 2 hours, less than about 1 hour, and less than about 30 minutes after administration to fasting subjects.

106. The method of claim 103, wherein the fibrate or a salt thereof is selected from the group consisting of a crystalline phase, an amorphous phase, a semi-crystalline phase, a semi-amorphous phase, and mixtures thereof.

107. The method of claim 103, wherein the effective average particle size of the fibrate particles is selected from the group consisting of less than about 1900 nm, less than about 1800 nm, less than about 1700 nm, less than about 1600 nm, less than about 1500 nm, less than about 1400 nm, less than about 1300 nm, less than about 1200 nm, less than about 1100 nm, less than about 1000 nm, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 200 nm, less than about 100 nm, less than about 75 nm, and less than about 50 nm.

108. The method of claim 103, wherein the composition is formulated for administration selected from the group consisting of oral, pulmonary, rectal, ophthalmic, colonic, parenteral, intracisternal, intravaginal, intraperitoneal, local, buccal, nasal, and topical administration.

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109. The method of claim 103, wherein the composition is a dosage form selected from the group consisting of liquid dispersions, oral suspensions, gels, aerosols, ointments, creams, controlled release formulations, fast melt formulations, lyophilized formulations, tablets, capsules, delayed release formulations, extended release  
10 formulations, pulsatile release formulations, and mixed immediate release and controlled release formulations.

110. The method of claim 103, wherein the composition further comprises one or more pharmaceutically acceptable excipients, carriers, or a combination thereof.

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111. The method of claim 103, wherein the fibrate or a salt thereof is present in an amount selected from the group consisting of from about 99.5% to about 0.001%, from about 95% to about 0.1%, and from about 90% to about 0.5%, by weight, based on the total combined weight of the fibrate or a salt thereof and at least one surface stabilizer, not  
20 including other excipients.

112. The method of claim 103, wherein the at least one surface stabilizer is present in an amount selected from the group consisting of from about 0.5% to about 99.999% by weight, from about 5.0% to about 99.9% by weight, and from about 10% to  
25 about 99.5% by weight, based on the total combined dry weight of the fibrate or a salt thereof and at least one surface stabilizer, not including other excipients.

113. The method of claim 103, comprising at least one primary surface stabilizer and at least one secondary surface stabilizer.

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114. The method of claim 103, wherein the surface stabilizer is selected from the group consisting of an anionic surface stabilizer, a cationic surface stabilizer, a zwitterionic surface stabilizer, and an ionic surface stabilizer.

5           115. The method of claim 114, wherein the at least one surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers,  
10 polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hypromellose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hypromellose phthalate, noncrystalline cellulose,  
15 magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde, poloxamers; poloxamines, a charged phospholipid, dioctylsulfosuccinate, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfate, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), decanoyl-N-methylglucamide; n-decyl  $\beta$ -D-glucopyranoside; n-decyl  $\beta$ -D-maltopyranoside; n-dodecyl  $\beta$ -D-glucopyranoside; n-dodecyl  $\beta$ -D-maltoside; heptanoyl-N-methylglucamide; n-heptyl- $\beta$ -D-glucopyranoside; n-heptyl  $\beta$ -D-thioglucoside; n-hexyl  $\beta$ -D-glucopyranoside; nonanoyl-N-methylglucamide; n-nonyl  $\beta$ -D-glucopyranoside; octanoyl-N-methylglucamide; n-octyl- $\beta$ -D-glucopyranoside; octyl  $\beta$ -D-thioglucopyranoside;  
20 lysozyme, PEG-phospholipid, PEG-cholesterol, PEG-cholesterol derivative, PEG-vitamin A, PEG-vitamin E, and random copolymers of vinyl acetate and vinyl pyrrolidone.



116. The method of claim 114, wherein the at least one cationic surface stabilizer is selected from the group consisting of a polymer, a biopolymer, a polysaccharide, a cellulosic, an alginate, a nonpolymeric compound, and a phospholipid.

117. The method of claim 114, wherein the surface stabilizer is selected from the group consisting of benzalkonium chloride, polymethylmethacrylate trimethylammonium bromide, polyvinylpyrrolidone-2-dimethylaminoethyl methacrylate dimethyl sulfate, hexadecyltrimethyl ammonium bromide, cationic lipids, sulfonium compounds, phosphonium compounds, quarternary ammonium compounds, benzyl-di(2-chloroethyl)ethylammonium bromide, coconut trimethyl ammonium chloride, coconut trimethyl ammonium bromide, coconut methyl dihydroxyethyl ammonium chloride, coconut methyl dihydroxyethyl ammonium bromide, decyl triethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride bromide, C<sub>12-15</sub>dimethyl hydroxyethyl ammonium chloride, C<sub>12-15</sub>dimethyl hydroxyethyl ammonium chloride bromide, coconut dimethyl hydroxyethyl ammonium chloride, coconut dimethyl hydroxyethyl ammonium bromide, myristyl trimethyl ammonium methyl sulphate, lauryl dimethyl benzyl ammonium chloride, lauryl dimethyl benzyl ammonium bromide, lauryl dimethyl (ethenoxy)<sub>4</sub> ammonium chloride, lauryl dimethyl (ethenoxy)<sub>4</sub> ammonium bromide, N-alkyl (C<sub>12-18</sub>)dimethylbenzyl ammonium chloride, N-alkyl (C<sub>14-18</sub>)dimethyl-benzyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium chloride monohydrate, dimethyl didecyl ammonium chloride, N-alkyl and (C<sub>12-14</sub>) dimethyl 1-naphthylmethyl ammonium chloride, trimethylammonium halide, alkyl-trimethylammonium salts, dialkyl-dimethylammonium salts, lauryl trimethyl ammonium chloride, ethoxylated alkyamidoalkyldialkylammonium salt, an ethoxylated trialkyl ammonium salt, dialkylbenzene dialkylammonium chloride, N-didecyldimethyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium, chloride monohydrate, N-alkyl(C<sub>12-14</sub>) dimethyl 1-naphthylmethyl ammonium chloride, dodecyldimethylbenzyl ammonium chloride, dialkyl benzenealkyl ammonium chloride, lauryl trimethyl ammonium chloride, alkylbenzyl methyl ammonium chloride, alkyl benzyl dimethyl ammonium bromide, C<sub>12</sub> trimethyl ammonium bromides, C<sub>15</sub> trimethyl

ammonium bromides, C<sub>17</sub> trimethyl ammonium bromides, dodecylbenzyl triethyl ammonium chloride, poly-diallyldimethylammonium chloride (DADMAC), dimethyl ammonium chlorides, alkyldimethylammonium halogenides, tricetyl methyl ammonium chloride, decyltrimethylammonium bromide, dodecyltriethylammonium bromide, 5 tetradecyltrimethylammonium bromide, methyl trioctylammonium chloride, POLYQUAT 10™, tetrabutylammonium bromide, benzyl trimethylammonium bromide, choline esters, benzalkonium chloride, stearylalkonium chloride compounds, cetyl pyridinium bromide, cetyl pyridinium chloride, halide salts of quaternized polyoxyethylalkylamines, MIRAPOL™, ALKAQUAT™, alkyl pyridinium salts; amines, amine salts, amine oxides, 10 imide azolinium salts, protonated quaternary acrylamides, methylated quaternary polymers, and cationic guar.

118. The method of any of claims 114, 116, or 117, wherein the composition is bioadhesive.

119. The method of claim 103, wherein the composition comprises hypromellose, dioctyl sodium sulfosuccinate, and sodium lauryl sulfate as surface stabilizers.

120. The method of claim 103, wherein administration of the fibrate composition does not produce significantly different absorption levels when administered under fed as compared to fasting conditions, when administered to a human.

121. The method of claim 120, wherein the difference in absorption of the fibrate composition of the invention, when administered in the fed versus the fasted state, is selected from the group consisting of less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, and less than about 3%.

122. The method of claim 103, wherein said  $T_{\max}$  of the fibrate is selected from the group consisting of less than about 5 hours, less than about 4 hours, less than about 3 hours, less than about 2 hours, less than about 1 hour, and less than about 30 minutes after administration to fasting subjects.

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123. The method of claim 103, additionally comprising administering one or more active agents selected from the group consisting of HMG CoA reductase inhibitors and antihypertensives.

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124. The method of claim 103, wherein the subject is a human.

125. The method of claim 103, wherein the method is used to treat a condition selected from the group consisting of hypercholesterolemia, hypertriglyceridemia, coronary heart disease, cardiovascular disorders, and peripheral vascular disease .

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126. The method of claim 103, wherein the method is used as adjunctive therapy to diet for the reduction of LDL-C, total-C, triglycerides, or Apo B in adult patients with primary hypercholesterolemia or mixed dyslipidemia.

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127. The method of claim 103, wherein the method is used as adjunctive therapy to diet for treatment of adult patients with hypertriglyceridemia.

128. The method of claim 103, wherein the method is used to decrease the risk of pancreatitis.

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129. The method of claim 103, wherein the method is used to treat indications where lipid regulating agents are typically used.

130. A therapeutic method comprising orally administering to a mammalian subject in need an effective amount of a composition comprising a fibrate or a salt thereof formulated in such a way as to provide a blood plasma concentration profile, after an initial dose of the composition, with a  $T_{\max}$  of the fibrate of less than about 6 hours.

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131. The method of claim 130, wherein the fibrate is fenofibrate or a salt thereof.

132. The method of claim 131, wherein administration of the fibrate composition does not produce significantly different absorption levels when administered under fed as compared to fasting conditions, when administered to a human.

133. The method of claim 132, wherein the difference in absorption of the fibrate composition of the invention, when administered in the fed versus the fasted state, is selected from the group consisting of less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, and less than about 3%.

134. A method of treating a subject in need comprising administering to the subject an effective amount of a composition comprising:

- (a) particles of a fibrate or a salt thereof having an effective average particle size of less than about 2000 nm; and
- (b) at least one surface stabilizer associated with the surface of the fibrate particles, wherein the surface stabilizer is categorized by the U.S. Food and Drug Administration as GRAS.

135. A method of treating a subject in need comprising administering to the subject an effective amount of a composition comprising:

- (a) particles of a fibrate or a salt thereof having an effective average particle size of less than about 2000 nm; and
- 5 (b) at least one surface stabilizer associated with the surface of the fibrate particles,

wherein the composition when administered in the fed state to a human is bioequivalent to the composition when administered in the fasted state to a human, as established by a 90% Confidence Interval of between 0.80 and 1.25 for both  $C_{\max}$  and  
10 AUC or a 90% Confidence Interval of between 0.80 and 1.25 for AUC and a 90% Confidence Interval of between 0.70 to 1.43 for  $C_{\max}$ .